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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

SWOPE, SHERIDAN

ART UNIT

PAPER NUMBER

1652

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8

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/045,545

Applicant(s)

MAINES, MAHIN D.

Examiner

Sheridan L. Swope

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 October 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 3-7 and 13-26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2 and 8-12 is/are rejected.
- 7) ☒ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

Applicant's election with traverse of Invention III, Claims 1, 2, and 8-12 as well as the selection of species actin microspike formation in Claim 2 and epithelial cells in Claim 11 in Paper No. 7 is acknowledged.

Traversal of restriction is based on the argument that Claim 1 is a generic claim while, Claims 2, 11, and 12 are dependent subgeneric claims. This is true and, in fact, all are linking claims. However, restriction is proper since the generic claim, Claim 1, is not allowable. The traversal is also based on the ground(s) that there would not be a serious burden on the examiner if restriction were not required. This is not found persuasive. Restriction practice is not governed by a close relationship between claims. 35 U.S.C. 121 allows restriction of inventions which are independent or distinct. The reasons Groups I-III are distinct are described in the prior action. Invention III has a different classification from Inventions I and II. In addition, although Groups I and II have the same major classification, they are distinct as they encompass distinct combinations of classification, for example Invention I encompasses class 435 subclass 7.21 while, Invention II encompasses class 435 subclass 180. These two inventions comprise distinct chemical entities and would, therefore, require separate searches. The restriction requirement is still deemed proper and is therefore made FINAL.

Claims 3-7 and 13-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected Inventions.

Specification

The abstract of the disclosure is objected to because the second sentence of the abstract is a run on sentence. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, and 8-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. For Claim 1, it is not clear whether the recited invention is a method of changing cellular structure by increasing intracellular biliverdin reductase (BVR) wherein BVR causes the change in cellular structure. Two additional interpretations are that either (i) conditions effective in modifying cellular structure also increase BVR or (ii) the conditions effective in modifying cellular structure are unrelated to increases in BVR. Since Claims 2 and 8-12 are dependent on Claim 1, Claims 1, 2, and 8-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite. Clarification is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Magnusson et al, 1999 (In IDS) as evidenced by Argiro et al, 1985. Magnusson et al teach an increase in cellular BVR upon culturing of rat superior ganglion (Fig 5a & b). Changes in the structure of superior ganglion cells is inherent to culture in vitro as evidenced by Argiro et al. Thus, Magnusson et al teach a method of increasing BVR levels wherein cellular structure is modified. Therefore,

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Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Magnusson et al, 1999 as evidenced by Argiro et al, 1985.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1 and 8-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lagarias et al, 1997 (In IDS) in view of Ausubel et al, 1997 and further in view of Panahian et al 1999 (In IDS). Lagarias et al teach that *Arabidopsis thaliana* transformed to express BVR displays elongated hypocotyls and smaller cotyledons (Fig 2), deficiency in phytochrome chromophore (Fig 3), and fewer rosette leaves (Table 2), all characteristics of changed cellular structure. Lagarias et al, do not teach increasing intracellular concentrations of BVR in mammalian cells in association with altered structure of said cells. Ausubel, 1997 teach that transfection of mammalian cells in vitro, including epithelial cells, using nucleic acids, plasmids, adenoviruses, and retroviruses to increase intracellular levels of an exogenous protein is standard in the art. It would have been obvious to a person of ordinary skill in the art to use the methods of Ausubel et al to increase intracellular levels of BVR in a mammalian cell. The use of the methods of Ausubel et al to express BVR in mammalian cells and motivation to do so is suggested by Panahian et al 1999 who teach that modulation of BVR expression is a possible new direction for protecting neurons against ischemic injury and oxidative stress (Abstract, lines 23-24). The expectation of success in using the methods of Ausubel et al to increase intracellular

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levels of BVR in a mammalian cell is high as these are standard methods in the art. Therefore Claims 1 and 8-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lagarias et al, 1997 in view of Ausubel et al, 1997 and further in view of Panahian et al 1999.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2 and 8-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 1, 2, and 8-12 recite a method of modifying cell structure comprising increasing the intracellular concentration of any BVR or a fragment or variant thereof. The specification, for example in Example 1, fails to describe the use of any specific form of BVR, including fragments or variants, in said method. Thus, Claims 1, 2 and 8-10 are rejected under 35 U.S.C. 112, first paragraph.

Claims 1, 2, and 8-12 are further rejected under 35 U.S.C. 112, first paragraph. The specification is enabling for modifying the size, actin microspike formation, and polarity of HeLa cells by expressing the exogenous BVR used in Example 1. However, Claims 1 and 8-12 are not reasonably enabled by the specification for modifying any characteristic of cell structure. In addition, Claims 1, 2, 8-12 are not enabled by the specification for modifying any mammalian cell. The specification does not enable any person skilled in the art to which it pertains, or with

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which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1 and 8-12 are so broad as to encompass modifying any characteristic of cell structure. Claims 1, 2, 8-12 are so broad as to encompass modifying any mammalian cell. The scope of each of these claims is not commensurate with the enablement provided by the disclosure with regard to the large number of structural characteristics of cells and extremely large number of mammalian cells broadly encompassed by the claims. Since the complement of proteins expressed by a cell determines its structural and functional properties, predictability of which proteins can be changed in a cell and obtain the desired utility of changing cellular structure upon increasing the intracellular concentration of BVR, requires a knowledge of and guidance with regard to which proteins are necessary, unnecessary, or inhibitory for the recited utility and a detailed knowledge of the ways in which each protein's function relates to the function of the mammalian cell. However, in this case the disclosure is limited to increased size, actin microspike formation, and polarity in HeLa cells.

While recombinant and screening techniques are known, it is not routine in the art to screen for alterations in multiple cellular proteins and/or multiple cell lines, as encompassed by the instant claims. Furthermore, which proteins can be altered with a reasonable expectation of success in obtaining the desired activity/utility are limited in any cell and the results of such modifications are unpredictable. In addition, one skilled in the art would expect any tolerance to alteration in expression of a single protein to diminish with each further protein altered e.g. multiple protein alterations in a single cell line.

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The specification does not support the broad scope of the Claims 1, 2, 8-12 which, encompasses all mammalian cells that change structure in any way upon an increased intracellular concentration of BVR. The specification does not support the broad scope of Claims 1, 2, 8-12 because the specification does not establish: (A) which mammalian cells, cell lines, and cell strains may be successfully used for the desired utility; (B) which proteins within a cell may be modified without effecting the ability of the cell to change structure in response to BVR; (C) the general tolerance, of the ability of the cell to change structure in response to BVR, to modification of cellular proteins and extent of such tolerance; (D) which of the enormous number of possible cell structure changes may be successfully analyzed; (E) a rational and predictable scheme, for selecting cells having a complement of proteins with an expectation of obtaining the desired utility; (F) a rational and predictable scheme, for selecting which cellular structure changes to analyze upon elevated expression of BVR; and (G) the specification provides insufficient guidance as to which of the essentially infinite possible choices of mammalian cells with essentially infinite variations in their complement of proteins and infinite variation in structure changes in said cells is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of mammalian cells, with essentially infinite variations in their complement of proteins, that are able to change their structure in response to increasing the intracellular concentration of BVR. Without sufficient guidance, determination of the identity of cells having the desired biological characteristics is unpredictable and the

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experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

Claims 1, 2, and 8-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of BVR molecules, a genus of mammalian cells, and a genus of cell structural changes wherein increasing the intracellular concentration of said genus of BVR molecules in said genus of mammalian cells, is associated with said genus of changes in cellular structure. The specification teaches the structure of no species of such BVR molecules, only a single representative species of such cells, and only three representative species of such structure changes. Moreover, the specification fails to describe any other representative species for the genus of BVR molecules by any identifying characteristics or properties other than the functionality of changing the structure of a mammalian cell. Furthermore, the specification fails to describe any other representative species for the genus of cells by any identifying characteristics or properties other than the functionality of being a mammalian cell that changes structure in response to BVR. The specification also fails to describe any other representative species for the genus of cell structure changes by any identifying characteristics or properties other than the functionality of being a structure change that occurs in a mammalian cell in response to BVR. Given this lack of description of representative species encompassed by the genera of the claims, the specification fails to sufficiently describe the claimed invention in such

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full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 703-305-1696.

The examiner can normally be reached on M-F; 8:30-5 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sheridan L. Swope, Ph.D.


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